ANNEX A: References

Hair and Glucose

a.

Hair protein glycation as a long-term index of blood glucose in diabetics.
Oimomi M, Igaki N, Masuda S, Hata F, Maeda Y, Matsumoto S, Baba S
Diabetes Res Clin Pract 1988 Oct 5:305-8

Abstract
We used furosine, which is derived from fructose-lysine and is a glycation product, to measure the extent of hair protein glycation in diabetic patients. We took hair samples that were 12 cm long, corresponding roughly to 1 year's growth. While the furosine levels in these samples correlated poorly with fasting plasma glucose (FPG) and with hemoglobin A1c (HbA1c) levels at the time of sampling, better correlations were observed between glycation and the year-long average values of FPG, HbA1c, and the conduction velocities in two peripheral nerves. The glycation levels in these samples may thus reflect the year-long average of the patient's blood glucose. Hair glycation may serve as a valuable indicator both of long-term blood glucose trends and of the relationship between diabetic complications and blood glucose.

b.

Clinical application of hair protein glycation in the assessment of blood glucose control and diabetic neuropathy.
Masuta S, Sakai M, Ohara T, Igaki N, Nakamichi T, Maeda Y, Hata F, Oimomi M, Baba S, Kobe J Med Sci 1989 Feb 35:1-9

Abstract
Glycation of hair protein was assessed in diabetic patients by the measurement of furosine, which is derived from fructose-lysine, a glycated lysine residue in protein. The level of furosine in 12-cm-long hair which grew over the course of one year was significantly better correlated with the mean values of four determinations of fasting plasma glucose (FPG) and four determinations of hemoglobin A1c, respectively, at the time of hair sampling. The level of glycation in hair, which corresponds to the time taken for hair growth, may represent the mean level of blood glucose during the time corresponding to the growth period. The values of motor nerve conduction velocity and sensory nerve conduction velocity were better correlated with the level of furosine in hair corresponding in the length to 1 year's growth than the levels of FPG and hemoglobin A1c at the time of the determination of nerve conduction velocity. These results suggest that hair glycation may serve as a valuable indicator both of

long-term blood glucose trends and of the relationship between diabetic complications and blood glucose.

c.

Glycation of hair protein in the assessment of long-term control of blood glucose.
Oimomi M, Masuda S, Igaki N, Nakamichi T, Hata F, Matsumoto S, Baba S
Jpn J Med 1988 Aug 27:277-80

Abstract
Glycation of hair protein was assessed in diabetic patients by the measurement of furosine, which is derived from fructose-lysine, a glycated lysine residue in protein. The level of furosine in 12-cm-long hair which grew over the course of one year was significantly better correlated with the mean values of four determinations of fasting plasma glucose (FPG) and four determinations of hemoglobin A1c (HbA1c) performed at three-month intervals than with FPG and the level of HbA1c, respectively, at the time of hair sampling. The level of glycation in hair, which corresponds to the time taken for hair growth, may represent the mean level of blood glucose during the time corresponding to the growth period. These results suggest that the determination of glycation in hair may be useful as an indicator of long-term control of blood glucose levels if appropriate lengths of hair are taken from the scalp.

d.

Glycosylation of hair: possible measure of chronic hyperglycaemia.
Paisey RB, Clamp JR, Kent MJ, Light ND, Hopton M, Hartog M
Br Med J (Clin Res Ed) 1984 Mar 288:669-71

Abstract
To determine whether hair is excessively glycosylated in diabetes mellitus 4 cm hair samples were taken proximally from behind the ear in 50 white non-diabetics and 46 diabetics. Hair glycosylation was assayed by a modification of the thiobarbituric acid reaction. Blood was taken from the diabetics at the same time for measurement of glycosylated haemoglobin concentration. The mean (1 SD) concentration of fructosamine (mumol/100 mg hair) was 0.054 (0.011) for normal hair. Glycosylation was not related to sex, age, or hair colour. The diabetics' hair was more heavily glycosylated (0.097 (0.045] than normal (p less than 0.01) and there was a correlation between hair glycosylation and the concentration of glycosylated haemoglobin in the diabetics ($r = 0.71$; p less than 0.01). Hair from non-diabetics showed a stable time related increase in glycosylation when incubated with glucose. Glycosylation of hair might provide a stable long term measure of tissue glycosylation, useful in the investigation of microvascular complications of diabetes mellitus.

Other Analytes in Hair

e.

A review book on the subject, demonstrating that many analytes can be detected in hair:

Drug Testing in Hair
Pascal Kintz Institut de Medicine Legale
ISBN: 0849381126
CRC Press Publication Date: 5/7/1996

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f.

Detection and measurement of analytes in Saliva:

no level of analyte just presence

Saliva as a Diagnostic Fluid
Annals of the New York Academy of Sciences
Volume 694 published September 1993
http://www.annalsnyas.org/content/vol694/issue1/

for example:
Saliva testing for drugs of abuse
E. J. Cone

Addiction Research Center, National Institute on Drug Abuse, Baltimore, Maryland 21224.

Annals of the New York Academy of Sciences, Vol 694, Issue 1 91-127, 1993
Saliva testing for drugs of abuse can provide both qualitative and quantitative information on the drug status of an individual undergoing testing. Self-administration by the oral, intranasal, and smoking routes often produces "shallow depots" of drug that contaminate the oral cavity. This depot produces elevated drug concentrations that can be detected for several hours. Thereafter, saliva drug concentrations generally reflect the free fraction of drug in blood. Also, many drugs are weak bases and saliva concentrations may be highly dependent upon pH conditions. These factors lead to highly variable S/P ratios for many of the drugs of abuse. Table 3 provides a compilation of experimental and theoretical S/P (total) ratios determined for drugs of abuse. Estimations of the theoretical S/P (total) ratios for acidic and basic drugs were based on the Henderson-Hasselbalch equation. Saliva pH was assumed to be 6.8 unless reported otherwise by the investigators. Generally, there was a high correlation of saliva drug concentrations with plasma, especially when oral contamination was eliminated. Assay methodology varied considerably, indicating that saliva assays could be readily developed from existing methodology. There are many potential applications for saliva testing for drugs of abuse. Table 4 lists several general areas in which information from saliva testing would be useful. Clearly, saliva drug tests can reveal the presence of a pharmacologically active drug in an individual at the time of testing. Significant correlations have been found between saliva concentrations of drugs of abuse and behavioral and physiological effects. Results indicate that saliva testing can provide valuable information in diagnostics, treatment, and forensic investigations of individuals suspected of drug abuse. It is expected that saliva testing for drugs of abuse will develop over the next decade into a mature science with substantial new applications.

g.

Steroid hormone analysis in human saliva
D. O. Quissell
Department of Basic Sciences and Oral Research, University of Colorado School of Dentistry, Denver 80262.
Annals of the New York Academy of Sciences, Vol 694, Issue 1 143-145, 1993
Despite the aforementioned complications, noninvasive saliva collection has provided the medical and research community with an excellent medium for the monitoring of plasma steroid levels. This noninvasive method has permitted the evaluation and assessment of a multitude of endocrine studies that would have been extremely difficult, if not impossible, using other more familiar methods.

h.

Immunoreactive substance P in human saliva. A possible marker of chronic pain
W. C. Parris, B. V. Sastry, J. R. Kambam, R. J. Naukam and B. W. Johnson

Department of Anesthesiology, Vanderbilt University Medical Center, Nashville, Tennessee 37232-2125.
Annals of the New York Academy of Sciences, Vol 694, Issue 1 308-310, 1993
In all patients and volunteers, the levels of immunoreactive SP measured in saliva were about 100 times higher than the levels measured in plasma. SP per mg protein was consistently lower in both plasma and saliva of chronic pain patients than in healthy volunteers. These findings suggest that a simple noninvasive objective method of determining SP in saliva may become useful in the evaluation and treatment of chronic pain.

i.

Lithium in Saliva

Contradicting observations as to the direct correlation between saliva and serum/plasma levels. The invention may have solved those contradictions.

Saliva lithium levels in children: their use in monitoring serum lithium levels and lithium side effects.
Perry R, Campbell M, Grega DM, Anderson L
J Clin Psychopharmacol 1984 Aug 4:199-202

Abstract
The reliability of saliva lithium levels in monitoring serum lithium levels in children taking lithium has rarely been studied, despite the potential usefulness of such a study and despite a number of adult studies focusing on the technique. In a study of 61 aggressive school-age children diagnosed as undersocialized, aggressive conduct disorder, a subsample of 21 children received lithium. Saliva lithium levels aided in monitoring side effects, and in 15 of the 21 children simultaneous saliva and serum lithium levels were done. These were highly correlated ($r = 0.83$) and the saliva to serum ratio was 2.53 across subjects. The results indicate that future work with larger numbers of children should study the ratio of saliva to serum lithium levels. Adult studies have shown that there is too great a variability in saliva to serum lithium level ratios to support the use of a fixed saliva to serum lithium ratio. This may not be the case in children. Seventeen children from the lithium subsample experienced 41 lithium-related side effects. Most children suffered side effects on relatively high doses of lithium, and those few who experienced side effects on low dosage had saliva lithium levels that were proportionately high. However, it remains unclear whether saliva lithium can be used to monitor side effects.

j.

Usefulness of saliva lithium estimation.
Verghese A, Indrani N, Kuruvilla K, Hill PG
Br J Psychiatry 1977 Feb 130:148-50